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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/01/2005

Sabine Eming

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JOYCE VON NATZMER
PEQUIGNOT + MYERS LLC
200 Madison Avenue
Suite 1901
New York, NY 10016

EXAMINER

SAOUD, CHRISTINE J

ART UNIT

PAPER NUMBER

1647

MAIL DATE

DELIVERY MODE

02/26/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/506,893	Applicant(s) EMING ET AL.	
	Examiner Christine J. Saoud	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 November 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-7,9-15 and 17-21 is/are pending in the application.
- 4a) Of the above claim(s) 17-20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 3-7, 9-15 and 21-22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Response to Amendment

Applicant's response of 27 November 2008 has been received. Claims 1, 10 and 12 have been amended and claims 21-22 have been added. Claims 1, 3-7, 9-15 and 17-22 are currently pending. Claims 17-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 12 February 2007.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Any objection or rejection of record which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

Applicant's arguments filed 27 November 2007 have been fully considered but are not persuasive.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-7, 9-15 and 21-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for alteration of a plasmin cleavage site by substitution of amino acids corresponding to positions 110 and/or 111 of VEGF165 in a VEGF molecule, does not reasonably provide enablement for alteration of positions corresponding to positions 109 or 112 for the reasons of record as applied to claims 1, 3-7, and 9-15. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant argues at page 11 of the response that the claims are not overly broad because 4 amino acids can be replaced or can be deleted and that the specification provides examples for the replacement of two of these for positions and for their specific use. Applicant's argument has been fully considered but is not persuasive.

The claimed invention is directed to VEGF molecules in which the plasmin cleavage site at amino acid positions 110/111 (corresponding to those positions in VEGF165) has been altered to prevent proteolytic degradation. The claims encompass mutation/deletion of amino acids 109 to 112 in this region of the molecule. However, amino acids 109 and 112 are not involved in this process, so there is no reasonable expectation that modification of these positions will have any biological effect on the molecule such that the VEGF molecule is not susceptible to plasmin degradation. It is not clear how the molecule should be altered at these amino acid positions to obtain a

VEGF molecule that is useful. Therefore, it would require undue experimentation to make and use the invention commensurate in scope with the claims, absent evidence to the contrary.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-7, and 9-15 and 21-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Keyt et al. (J. Biol. Chem. 271(13): 7788-7795, 1996) and Lauer et al. (J. Invest. Dermatol. 115: 12-18, 2000) in view of Market et al. (Protein Engineer.

14(10): 791-796, 2001) and U.S. Pat. No. 5,219,739 (Tischer et al.) for the reasons of record as applied to claims 1, 3-7 and 9-15.

Applicant argues that Market et al. is directed to proteases other than plasmin and that the activities and specificities of these proteases differ from plasmin, therefore, no inferences can be drawn with regard to the other proteases, in particular not plasmin and the person skilled in the art would also not have had any reasonable expectation of success. Applicant's argument has been fully considered, but is not persuasive.

Market et al. was cited for the technique of site-directed mutagenesis in order to provide proteolytic resistance to enzymatic degradation, not for any particulars of which amino acid to substitute or what position should be substituted. Keyt et al. was cited for the teaching of the amino acids which are involved in plasmin cleavage. At the time of the instant invention, it was well known that plasmin cleaves at dibasic amino acid pairs, therefore, there is a reasonable expectation that if either the amino acids at positions 110 or 111 (or both amino acids) are substituted such that they are no longer a dibasic pair, then the plasmin will not longer be able to cleave the protein. This concept was old and well known at the time of the invention, contrary to Applicant's assertion that the skilled artisan would not have had any reasonable expectation of success. Applicant's reliance on Market et al. for particular amino acids to be substituted at particular positions is misplaced since Market et al. was cited for the general technique of site-directed mutagenesis to provide proteolytic resistance to enzymatic degradation.

Therefore, the invention as a whole would have been *prima facie* obvious at the time it was made, absent evidence to the contrary.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine J. Saoud whose telephone number is 571-272-0891. The examiner can normally be reached on Monday-Friday, 6AM-2PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao can be reached on 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Christine J Saoud/

Primary Examiner, Art Unit 1647